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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/690,825	10/18/00	ALTIERI D	044574-5022-

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EXAMINER	
CANELLA,K	
ART UNIT	**PAPER NUMBER**
1642	17

DATE MAILED: 08/30/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/690,825	Altieri
Examiner	**Art Unit**
Karen Can lla	1642

-- The MAILING DATE of this communication appears on the cov r sh et with the c rrespond nce address --

Period for R ply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3 months* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-8 and 17-76* is/are pending in the applica

4a) Of the above, claim(s) *1-8, 19-38, and 41-59* is/are withdrawn from considera

5) ☒ Claim(s) *62, 74, and 76* is/are allowed.

6) ☒ Claim(s) *17, 18, 39, 40, 60, 61, 63-73, and 75* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirem

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *4*

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

1. Acknowledgment is made of applicants election, without traverse, of Group X, drawn to polypeptides, peptidomimetics and vaccines comprising polypeptides.

2. Regarding applicants objection to the response time, it is noted that 30 days was set forth as the response period. The MPEP 809.02(a) specifies a response period of not less than 30 days, thus, the shortened statutory period indicated in the office action summary of Paper No. 5 was not incorrect.

3. Claims 17 and 18 have been amended. Claims 60-76 have been added. Claims 9-16 have been canceled. Claims 1-8, 19-38, 41-59, drawn to non-elected inventions, are withdrawn from consideration. Claims 17, 18, 39, 40 and 60-76 are examined on the merits.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 64-73 and 75 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(A)Claims 64-68 and 70 recite 'comprising at least X amino acids of SEQ ID NO:34' without stating that the claimed amino acids are contiguous in SEQ ID NO:34. For purpose of examination, the claims will be read as 'at least X contiguous amino acids of SEQ ID NO:34'.

(B)The recitation of "Pro^{73}" in claim 75 lacks proper antecedent basis in claim 74.

(C)The recitation of 16.5 KDA in claim 60 is indefinite without a description of how the molecular weight was obtained. For purpose of examination, 16.5 KDA will be read as determined by SDS-PAGE under reducing conditions.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 18, 39, 40, 63-68, 70, 72 and 73 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the Survivin protein, the BIR domain, the BCOOH domain, does not reasonably provide enablement for random fragments of the Survivin protein, and fusion proteins there of, vaccines comprising the Survivin protein or fragments thereof, or homologs and peptidomimetics of SEQ ID NO:4. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to the invention commensurate in scope with these claims.

(A)As drawn to vaccines comprising Survivin protein, fragments thereof and fusion proteins comprising Survivin protein and fragments thereof.

Claims 39 and 40 are drawn to vaccines comprising the Survivin protein or fragments thereof sufficient to evoke an immune response. Claim 72 is drawn to fusion proteins of Survivin and fragments thereof. The specification teaches that the Survivin protein, expressed in actively proliferating transformed cells, is undetectable in adult tissues, with the exception of normal PBMC (pg. 16, lines 16), but becomes prominently expressed in human cancers ranging from lung, colon, breast, pancreas, prostate and high-grade non-Hodgkin's lymphoma. The specification thus fails to provide enablement for how one of skill in the art could use the Survivin protein, fragments or fusion proteins thereof in a vaccine to generate an efficacious immune response against cancer in light of the fact that the Survivin protein is a normal constituent of peripheral blood mononuclear cells. Overcoming the bodies tolerance to epitopes which could be expressed in the context of MHC class I would result in an immune response against normal PBMC generating an autoimmune disorder. The specification fails to teach any qualitative or quantitative differences between MHC class I processing in cancer cells vs normal PBMC that would facilitate selection of a particular epitope or fragment of Survivin for use as a immunotherapeutic agent (for example see: Skipper et al, Journal of Experimental Medicine,

1996, Vol. 183, pp. 527-534). If the Survivin polypeptide is expressed on the surface of the cancer cell by some other mechanism apart from Class I processing of endogenous proteins, it must be available in sufficient quantity and in appropriate context (Hiraki et al, Clin Cancer Res, 1999, Vol. 5, pp. 933-936) for a reasonable probability of immunorecognition and must not be masked by other antigens on the cancer cell or by over glycosylation or other protein modification (Welt and Ritter, Seminars in Oncology, 1999, vol. 26, pp. 683-690, Blumenthal et al, Int. J. Of cancer, 1992, Vol. 51, pp. 935-941). It is well know in the art that cancer patients have antibodies that react with their own tumor antigens in vitro (Becker et al, Int Immunol., 1993, Vol. 5, pp. 1501-1508). However, cancer patients often fail to mount an immune response to their own tumors. It is possible that tumor cells in vivo evade immune detection by mechanisms not well understood in the art (for example, Paul et al, PNAS, vol. 14, pp. 4501-4505 and Ada, G., Immunology and Cell Biol, 1999, vol. 77, pp. 180-185). Thus it cannot be anticipated that Survivin proteins, fragments and fusion proteins thereof would be useful in a vaccine against cancer. Without further guidance in the specification regarding these issues, one of skill in the art would be subject to undue experimentation without reasonable expectation of success in order to use the Survivin proteins, fragments and fusion proteins thereof in a vaccine.

(B)As drawn to substituted homologs and peptidomimetic of SEQ ID NO:4

Claim 18 is drawn to a polypeptide comprising SEQ ID NO:4, conservatively substituted homologs and small molecule peptidomimetics thereof. The specification teaches that SEQ ID NO:4 (amino acids residues 65-84) of SEQ ID NO:34 is the portion of the Survivin protein responsible for interaction with other molecules in the cell (pg. 70, lines 17-21). The specification teaches that unlike other IAP proteins, Survivin does not bind caspases (pg. 14, lines 17-19). Thus the binding partner of SEQ ID NO:4 is not disclosed by the specification. Given this deficiency of disclosure, one of skill in the art would be subject to undue experimentation in order to make homologs and peptidomimetics which would function in the same manner as SEQ ID NO:4 with regard to the binding of undisclosed cellular protein.

(C)As drawn to random fragments of SEQ ID NO:34 and fusion proteins comprising a ring-finger domain.

Claim 73 is drawn to a fusion protein comprising an unspecified fragment of SEQ ID NO:34 with a C-terminal ring finger protein, and disclosed domains of the Survivin protein (coiled-coil and BIR) fused with a C-terminal ring finger protein. The specification teaches that the BIR domain is the minimal region responsible for the inhibition of apoptosis (pg. 63, lines 13-21). The specification further teaches that the Survivin protein is devoid of a C-terminal ring-finger domain common to other IAP proteins. The specification teaches that a Survivin chimeric molecule comprising a C-terminal ring-finger domain was recombinantly generated, but found to be inactive at inhibiting apoptosis. Therefore, one of skill in the art would not know how to use a C-terminal ring finger fusion protein comprising Survivin or fragments thereof.

Claims 64-68 and 70 are drawn to polypeptides comprising unspecified fragments of SEQ ID NO:34. The specification teaches the BIR domain and the BCOOH domain of Survivin. As stated in the paragraph, supra, the specification teaches that the BIR domain is the minimal region responsible for the inhibition of apoptosis. The specification further teaches that truncated Survivin lacking the BCOOH domain was less effective at inhibiting apoptosis that non-truncated Survivin (pg. 71, lines 2-4). However, the specification does not teach a function for unspecified fragments of SEQ ID NO:34 comprising 10, 15, and 17 amino acids. The specification is only enabling for fragments consisting of the 20 amino acids of SEQ ID NO:4, the 40 amino acids of the BCOOH domain, and the 70 amino acids of the BIR domain. Clearly the specification does not provide any teachings for how to select or use all possible 10, 15, 20, 40, and 70 amino acid fragments of SEQ ID NO:34 other than in the specifically disclosed BIR and BCOOH domains and SEQ ID NO:4. Without further guidance from the specification, one of skill in the art would be subject to undue experimentation in order to use the claimed amino acid fragments to the full scope of the claims.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

9. Claims 17, 60 and 61 are rejected under 35 U.S.C. 102(e) as being anticipated by Korneluk et al (USP 6,107,041). Claim 17 is drawn in part to variants and fragments of SEQ ID NO:34 which retain the ability to inhibit apoptosis. Claim 60 is drawn to an isolated polypeptide of the IAP family, wherein the peptide has a molecular weight of 16.5 KDA and inhibits apoptosis. Claim 61 embodies a human IAP polypeptide. Korneluk et al disclose expression of the cDNA encoding the BIR domains from human xiap for the inhibition of apoptosis (column 24, lines 27-29). Korneluk disclose that human xiap is a IAP polypeptide and that each BIR domain is 70 amino acids (column 1, lines 40-42), therefore, expression of the two domains would results in a protein which would exhibit the same molecular weight as Survivin. Thus, Korneluk fulfills the requirement of a fragment of an allelic variant of SEQ ID NO:34 retaining the ability to inhibit cellular apoptosis and a human polypeptide having a molecular weight of 16.5 KDA which inhibits apoptosis.

Conclusion

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Canella whose telephone number is (703) 308-8362. The examiner can normally be reached on Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

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Patent Examiner, Group 1642
August 26, 2001

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